PHYSIOLOGICAL AND PSYCHOLOGICAL RESPONSES TO STRESS IN NEUROTIC PATIENTS

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INTRODUCTION

At the beginning of the war, part of the Maudsley Hospital moved to Mill Hill School, and a neurosis centre of 550 beds was established. During the six years of war some 20,000 neurotic patients, both forces and civilian, were treated at this centre. Within the centre a special unit for the study of forces patients with effort syndrome (E.S.) was set up. This unit was in existence from 1939 to 1945, and during this period 2,324 cases of E.S. were treated. The writer was associated with this unit throughout, working in association with a cardiologist (Paul Wood (1)), and with other psychiatrists (Lewis (2) Guttmann (3) Gillespie (4)). Much of the material brought together in this thesis has already been published (Jones (3) (5) (6) (7) (8) (9) (10) (11) (12) (38) (43). During most of the war years the writer was in receipt of a Medical Research Council grant.

During the first world war, Sir Thomas Lewis (13) made a careful study of E.S., and in 1940 he published a revised edition of his monograph: I would like to quote from the introductory remarks of this edition. "During the last war sickness referred by medical officers of the Services to disturbances of the cardiovascular system was a chief malady. One such case was numbered for every four cases of wound. Cardiovascular disturbances followed chest complaints as the second largest group of medical ailments; it comprised in the terminology of the time, two chief groups, namely, those invalided for "disordered action of the heart" (D.A.H.), and those invalided for

"valvular disease of the heart" (V.D.H.). "Irritable heart", an earlier term than "disordered action of the heart", dates from Da Costa and the American Civil War. Da Costa belived that it led up to enlargement and failure of the heart; but time has not endorsed his view. What he described was not a disease, but a series of symptoms found in many different states. Their reference to the heart is a grave objection to each term, for it maintains among those who use it the presumption that there is a cardiac malady, and among patients each awakens serious apprehension. Because these designations were impracticable from these standpoints, and because they implied a disease, rather than a syndrome, I discarded them during the last war and introduced the more appropiate and less committal term "effort syndrome"; the term was universally adopted in this country and is still in general use. The condition to which it refers forms the chief subject matter of this book.

The magnitude of the problems presented by this condition, from the standpoints of army wages, invalidism, and pensioning will be realised when it is known that not less than 70,000 soldiers had reported sick and were classed as cardiovascular by the summer of 1918; and 44,000 cases of "effort syndrome" became pensioners. Actually, no more than one out of six of these soldiers suffered from disease of the heart, the rest were "effort syndrome" cases. The problem is the same in this war as in the last; and, if this war continues as the last did, it will not be of much less magnitude than it was in that".

Lewis considered the etiology of E.S. to be partly physical (mainly following infections), and partly constitutional (poor physique), nervous temperament etc.), but although admitting the importance of psychological factors, he did not stress these --- to quote (page 13). "In my view (such) nervous symptoms are not to be regarded as parts of the "effort syndrome".

They are certainly not essential to it, for most cases are without them; they are added to the syndrome, and are of sufficient frequence to leaven the whole group. A matter more relevant to the present discussion is to know if the symptoms properly belonging to the "effort syndrome", namely, persistently increased heart rate and blood pressure, and exaggerated breathlessness on effort, can arise directly out of anxiety states; it seems probable that they can, and that abnormal anxiety must be regarded as a real and important contributing cause in given patients". Physiological studies by Lewis and his collaboratora ((16) (17) (18)) by Haldane and his associates ((19) (20) (21)), and by Briggs (22) demonstrated clearly that E.S. patients responded poorly to exercise, and showed various physiological anomalies, but the etiology of the condition still remained obscure.

Between the two wars little was done to study the problem, but in 1937 Hick et al (24) brought forward impressive evidence in support of Haldane's earlier suggestion that the symptoms of E.S. were due to anoxaemia of effort, and in 1938 Soley and Shock (23) suggested that the symptoms of E.S. were due to hyperventilation alkalosis.

When we started to study the problem of E.S. there were two main schools of thought: the cardiologists (Lewis (13) Parkinson (14) White (15)) who still felt that the etiology of E.S. when not due to definite organic factors, was unknown, and the psychiatrists who were inclined to deny the existence of E.S. as an entity, and thought of it as a particular form of anxiety state. The cardiologists point of view is well expressed by Parkinson (14). Speaking of E.S. he states "Its true nature is not yet known, but the full picture which bulks in war is only sporadically encountered in peace-time. Tentatively, I would define Effort Syndrome as a functional circulatory disease, most evident on exertion, unmasked or produced by war service. It is hoped that the

experience of this war will provide a better name, a more satisfactory definition, and a clearer understanding of this condition".....

"In the present war, conditions so far seem to have produced a preponderance of the psychoneurotic type, and a greater proportion of those who had similar symptoms in civil life. Indeed some current opinion is inclined to the view that effort syndrome is simply a psychoneurosis. It is not certain how far this definition will carry us, because the term can be so readily applied to any form of ill-health which is imperfectly understood and unaccompanied by organic signs. After all, psychological variations and faults in healthy people are common enough. It could only be a bar to medical progress if psychoneurosis (or psycho-somatic disease) remained a label and became a dumping ground for most unexplained illness, much as did 'Neurasthenia' in the past. It is still to be decided how far psychotherapy is rational and effective treatment; besides, an explanation for the predominance of circulatory symptoms, the relation to effort, and the relative uniformity of the clinical picture is not yet forthcoming. Certainly the time is ripe not only for psychological but for other investigations, as it would appear that autonomic, nervous, endocrine, respiratory and metabolic factors may also operate in effort syndrome, and will also engage the attention of the physician seeking a wider conception of its essential features. Doubtless this expanded approach has much to commend it, and will deepen and broaden our vision of what is at present obscure in the rationale of Effort Syndrome".

The E.S. unit at Mill Hill started at the end of 1939 with a psychiatrist and a cardiologist working in collaboration. We had no fixed view point although each worker naturally approached the problem in a somewhat different manner determined partly by his own personality and training. The cardiologist (Paul Wood) remained with us for eighteen months, at the end of which time

he had decided that the problem was a psychiatric and not a cardiological one. In his Goulstonian lectures (1) he stated "It is urged that the diagnosis of "effort syndrome" be dropped, a proper psychiatric diagnosis is nearly always available; if attention is called to the presence of effort intolerance, let effort intolerance be added in brackets".

From the psychiatric point of view there was no advantage in retaining the diagnosis of effort syndrome, and as the war progressed the number of cases sent into Mill Hill by the army psychiatrists with this diagnosis progressively diminished --- 732 in 1940; 650 in 1941; 531 in 1942; 220 in 1943; 99 in 1944. There was no reason to suppose that the syndrome had become less frequent, but presumably familiar psychiatric diagnoses were being used instead.

The growing realisation that E.S. was not an entity did not diminish our interest in the subject of effort intolerance, or in the various anomalies of vegetative function found in these cases. It was still far from clear what the effort intolerance was due to, or how this disability could be measured objectively (if indeed it was present at all).

This thesis is concerned mainly with a study of some of the physiological functions of neurotic cases with effort intolerance. It is convenient, for research purposes to retain the use of the term 'effort syndrome' (E.S.) to indicate cases with effort intolerance as distinct from other types of neuroses --- the alternative would have been to use the psychiatric diagnosis and add 'with effort intolerance' in brackets.

The term, effort syndrome, as used here, refers to a relatively excessive response to effort as manifested by breathlessness, palpitation, and subjective feeling of fatigue on even mild exercise, along with excessive vegetative liability on emotional excitement, e.g.; sweating, palpitation, giddiness, etc., as described by the patient or objectively observed. If there be a known organic

cause, then that diagnosis is, of course, used in preference to the term effort syndrome. "Syndrome" is a descriptive term generally used to avoid premature aetiological conception; there is apparently no common aetiology to E.S.; and as a descriptive term is generally favoured, the American preference for the term "neurocirculatory asthenia" seems reasonable.

In the majority of E.S. patients seen here, constitutional (including personality) factors would appear to be more important than psychogenic factors; thus when a breakdown occurs there may be no pronounced affective disorder, and no adequate psychopathology to explain the illness. From this it follows that existing psychiatric classifications, based on aetiological or descriptive grounds, would be difficult to apply. It therefore seems reasonable to use a classification which takes into account constitution and personality more fully than do existing classifications. One can divide the E.S. material into three broad groups: (1) Where the poor physical endowment is the primary factor in producing symptoms. Here we are simply dealing with a poor machine, which shows excessive response to physical effort. Here the patient has effort intolerance which has been present since earliest recollection. (2) As above, but the patient responds in a neurotic manner to his constitutional inferiority. In this sense there is a psychological aetiology, but the constitutional factor is the basic one. The emotional reaction may take any form, depending on the personality and may simply amount to displeasure. Here the patient feels that he has an effort intolerance, but his disability may actually be less than he believes it to be. Such patients usually give a history of effort intolerance since childhood, but the mere disability of Group 1 frequently changes under stress to the neurotic attitude of Group 2. (3) Primarily neurotic. Here the usual aetiological factors determining a neurosis will apply. The form may be determined by the constitutional physical inferiority which, if present, colours

the whole picture, but is of only secondary importance; or it may be wholly psychogenically determined. Such "illness" tends in our experience to be of comparatively recent origin, and is particularly prone to result from the emotional and physical stresses of wartime.

By neurosis is meant an upset of the normal harmonious functioning of the mind and body resulting from some personal inadequacy to meet a psychological situation or problem. Poor general health, weak physical constitution, low intelligence, etc., may predispose to such a neurosis, but these are in themselves not enough; the individual has failed to meet the demands of his environment or of his conscience, and a conflict has been set up. Thus, the Group 1 E.S. has the symptomatology of the other two groups, but his physical limitation has been satisfactorily met and presents no handicap, so he has no neurosis. The opposite is true of Group 2 E.S.

This division into 3 groups of E.S. proved convenient, but unfortunately only an occasional group 1 E.S. was seen (from the definition it is clear that they would only be discovered when examining a large random sample of controls because they do not regard themselves as ill, and therefore would not report sick), and no detailed study of this group has been possible.

PROBLEMS STUDIED IN THIS THESIS

1. Had the E.S. patients a poor exercise response compared with a normal control group? Judged by the subjective accounts of E.S. patients there was a real disability, but could this be assessed objectively.

2. What method or methods were most suitable for demonstrating objectively this disability (if present)?

3. As E.S. was not a psychiatric entity it was important to compare neurotic patients showing poor exercise response with other neurotic patients not complaining of this disability: poor exercise response might be closely correlated with neuroses showing anomalies of vegetative function -e.g.- somatic anxiety symptoms, or might be an attribute of neuroticism in general.

4. How important was the subjective attitude to physical work in the E.S. patient? Does he in fact have any effort phobia?

5. How did E.S. and other neurotic patients respond to stresses other than physical exercise -e.g.- cold, pain, emotional excitement, and persistence?

6. As the ultimate aim of all research in medicine must be the benefit of the patient, how did the facts elicited influence the treatment of poor exercise response in neurotic patients, and of certain other types of neurotic patients not complaining of effort intolerance?

(As most of the statistics worked out in this thesis are based on small samples (twenty or less) we have regarded $P < 0.01$ as significant and $P < 0.05$ as probably significant.)

Fig. 1: SHOWING BICYCLE ERGOMETER AND POSITION ADOPTED WHEN CYCLING.

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RESPONSE TO STRESS

1. EXERCISE RESPONSE

Under this heading are included four different degrees of stress.

(a) Standard Work which represents moderately hard work (6,750 ft.lbs. of work per min.)

(b) Maximal Work which means working to complete exhaustion.

(c) Light Work (4,500 ft.lbs. of work per min.)

(d) Minimal Work Virtually no work being done by the subject.

(a) STANDARD WORK

An ergometer was made by adapting an old bicycle and fracture bed (see Fig.1).

The ergometer consisted of a bicycle-chain wheel and pedals connected by the frame to the ground wheel which had a friction band with weights and a spring balance. The whole was supported by two uprights off the end of the bed so that the subject could pedal as he lay on the bed; though unorthodox the position was comfortable, and facilitated the collection of blood samples. We have used a standard exercise throughout: pedalling at 42 revolutions per minute, the friction of the brake band being equivalent to a weight of 9 lbs., and the subject doing 6,750 ft.lbs. of work per minute for five minutes. In deciding on the amount of work to be done for the standard exercise we chose the heaviest work which could be done satisfactorily by the worst of the E.S. material.

1. Pulse Response to Standard Work.

Material — For this study we used a random sample of 20 healthy men from a nearby barracks. They were all tradesman (fitters), and in good health at the time of testing. None had a past history of serious illness affecting the respiratory or circulatory systems. Each had a short interview with the

psychiatrist and none showed any evidence of frank neurosis. Their weights ranged from 120 to 154 lbs. with a mean of 143.4lbs. Their ages ranged from 18 to 35 with a mean of 24.7.

Ten patients with a characteristic history of E.S., and 10 patients with anxiety states and somatic anxiety symptoms but no complaint of poor exercise response were chosen. Six of the E.S. patients described effort intolerance and symptoms of excessive vegetative liability on excitement since childhood (Group 2 E.S.) In the remaining four E.S. patients their symptoms dated from recent years --- during army service (Group 3 E.S.). All 20 patients were free from any demonstrable organic disease and had no history of serious respiratory or circulatory illness at any time in their lives. The E.S. patients' weights ranged from 132 to 164lbs. with a mean of 143.6lbs., and their ages ranged from 24 to 36 with a mean of 29. The comparable figures for the anxiety states were 133 to 161lbs. with a mean of 143.9lbs., and 23 to 36 with a mean of 30 years.

The controls, being craftsmen, were leading relatively sedentary lives and had less physical training, marching, etc., than the patients.

Method.—Standard work on the bicycle ergometer was used. The subjects did the tests on three successive days before any recorded test was made. Many attempts have been made to devise a reliable test of physical efficiency from the pulse response after exercise. This method, however, can never be very accurate as cardiac rate is only one factor which determines cardiac output, the latter being what one would really like to measure. However, after moderate or severe physical exercise, a characteristic curve is obtained in which the major pulse decrement occurs within the first four minutes, and then flattens out rapidly.

Our proceedure has been to count the pulse rate for a full minute for

TABLE 1

COEFFICIENT OF CORRELATION FOR PULSE RESPONSE (TREATED IN VARIOUS WAYS) TO STANDARD WORK, PERFORMED ON 2 SUCCESSIVE DAYS.

	20 Normal Controls		20 E.S. + Anxiety States	
	Correlation coefficient	Standard error	Correlation coefficient	Standard error
1. Resting pulse.....	0.605	.142	0.813	.076
2. First minute post exercise.....	0.512	.165	0.724	.103
3. Second minute post exercise.....	0.536	.159	0.691	.117
4. Third minute post exercise.....	0.514	.165	0.692	.117
5. Resting pulse minus first min. post exercise.....	0.382	.191	0.564	.153
6. 1,2,3,4,9 mins. minus resting pulse X 5 ..	0.665	.125	0.512	.165
7. 1,2,3,4,9 mins. minus resting pulse.....	0.581	.148	0.550	.156
8. 1,9 mins. minus resting pulse X 2	0.512	.165	0.462	.175
9. 1,2,3,4,9 mins. post exercise.....	0.562	.153	0.667	.124

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the ten successive minutes immediately following the cessation of exercise. The test was always repeated on successive days. Much trouble was taken to ensure standard conditions, and if necessary the subject rested more than thirty minutes before starting exercise if there was any difficulty in obtaining a constant resting pulse rate. / Table 1 shows the retest reliability (rank correlation) of various ways of expressing the pulse response to standard work on successive days. The E.S. patients and anxiety states are taken together as one group of 20. It will be seen that the resting pulse and peak pulse (for the minutes immediately after the cessation of exercise) correlate better in the E.S. plus anxiety groups (resting ρ = 0.813 $\pm$ .076 SE; peak ρ = 0.724 $\pm$ .103 SE) than in the controls (resting ρ = 0.605 $\pm$ .142 SE; peak ρ = 0.512 $\pm$ .165 SE).

Of the various ways of expressing the pulse figures shown in Table 1 no one method gives an outstandingly high correlation in both controls and E.S. plus anxiety states. We have paid more attention to one method which we have called the "Pulse Area" than the other methods available because it takes more account of the physiological changes occuring throughout the recovery period. It is obtained by adding the pulse figure for the first four minutes after the cessation of exercise, and the mean of the last three minutes counted (eight, nine, and ten minutes) and subtracting five times the resting pulse (see Table 1, Method 6). We have used it for some years now, and believe it to be the most accurate method of expressing the pulse response to moderate exercise.

Table 1

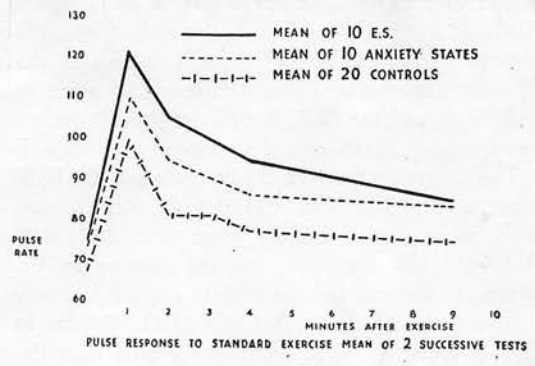

FIG. 2

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Results —Figure 2 shows graphically the pulse response of the various groups to standard work. All figures represent the mean of two tests done on successive days. For the 20 normal controls, the mean resting pulse was 67, and the mean pulse figures for the first four minutes after standard work were 100, 82, 81, 79. The means of the eighth, ninth and tenth after exercise were added together and averaged, the figure obtained being 76. The corresponding figures obtained for the 10 E.S.patients were 73, 121, 106, 100, 95, and 85, and for the 10 anxiety states, 72,110,97,91,88, and 84. Figure 2 shows how, when the results are plotted, the curves of the three groups are almost parallel. The greater pulse rise immediately after exercise in the E.S. patients and anxiety states compared with the controls are maintained, and result in a much slower decrement. Fig. 2.

The "Pulse Area" (see Method) is probably the best method for quantitating the pulse figures after standard work. It is obtained by adding the five pulse figures --- the first four minutes after exercise and the mean of the eigth, ninth, and tenth minutes, and subtracting five times the resting pulse. The difference between the Controls and E.S. patients for the mean pulse area is significant (Critical ratio (c.r.) 4.4; $P < .01$). The mean pulse area for the controls is 85.35 ± 36.0 s.d., while that for the 10 E.S. patients is 150.7 ± 36.73 s.d. The difference between controls and the 10 anxiety states is less marked (c.r. 2.08; $P < .05$). The mean pulse area for the anxiety states was 116.45± 34.7 s.d. Comparing the controls with the 10 E.S. patients plus the 10 anxiety states, significant difference is again obtained (c.r. 3.95;$P < .01$), the mean pulse area for the 20 patients being 135 ± 40.69 s.d.

The above group of 20 normal controls, 10 anxiety states with somatic but no complaint of effort intolerance symptoms, and 10 E.S. patients, were enlarged to form a group of 12 Group 2 effort syndromes (i.e., cases with a lifelong history of poor exercise response

TABLE 2

Significance of the Difference of the Means in Pulse Area, Between the Normal Control Group and 5 Different Groups of Neurotic Patients, for 5 Minutes Immediately Post (Standard) Exercise.

	Mean Pulse Area	S.D.	C.R.	P
20 normal controls	86	35.8		
12 E.S. Group 2.....	145	30.6	4.9	<0.01
15 E.S. Group 3	150	66.3	3.3	<0.01
10 somatic anxiety	116	34.7	2.1	<0.03
12 hysterics	100	30.5	1.1	<0.15
10 anxiety states	166	33.2	5.8	<0.01
Total 59 Neurotics	136	42.7	5.0	<0.01

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and excessive vegetative lability on excitement): 15 Group 3 effort syndromes (i.e. patients whose effort intolerance has developed as part of a neurosis, in contrast to the more "constitutional" Group 2 effort syndrome); 10 patients with mild anxiety states of a chronic nature who had no somatic anxiety symptoms, and no complaint of effort intolerance; 12 cases with conversion hysteria of the more chronic type with no clinical evidence of anxiety.

Table 2

Results:

Pulse Area — As will be seen from Table 2, the group of hysterics (c.r. 1.1; P<0.1 does not appear to differ significantly from the normal controls. The most striking differences are found in the anxiety states (c.r. 5.8; P < .01), and in the E.S. Group 2 (c.r. 4.9; P < .01). The mean pulse area for the 20 controls was 86 ± 35.8 s.d., and for the total 59 neurotic patients 136 ± 42.7 (c.r. 5.0; P < .01).

2. Metabolic Response to Standard Work.

The choice of method for measuring the metabolic increase brought about by exercise presents very great difficulties. Knipping (26) believes that the most satisfactory technique is to use a spirometer to which O_2 is added at the rate sufficient to keep the level of the spirometer constant. The rate of O_2 inflow into the closed circuit then equals the O_2 consumption. He increases the work load progressively until the maximum rate of O_2 intake is reached: this value is reached after two or three minutes and the work is interrupted after another two or three minutes. We experimented with this technique but were unable to have a satisfactory apparatus built in wartime, and in any case when using an improvised machine, found that it was unsatisfactory to have neurotic patients breathing into a closed circuit during exercise.

Ideally, one would like to compare the efficiency of muscular work in the three groups we have studied. Simonson and Enzer (27) in their excellent review of the physiology of muscular exercise and fatigue in disease discuss the whole problem adequately. The "coefficient of efficiency" $\frac{W}{Ew-R}$ (W = amount of work done; Ew = the total energy expenditure; R = the energy expenditure during

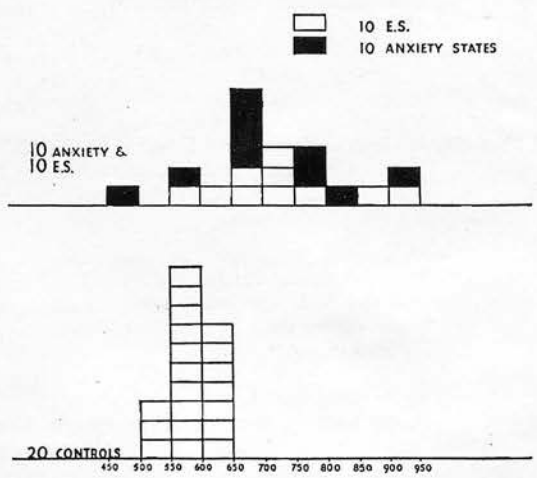
purpose by increasing the risk of provoking emotional reactions.

For the actual test the patient was rested for half an hour before exercising.

The subject then cycled for five minutes as above, and fifteen seconds before the completion of exercise the mouthpiece of the Douglas Bag was inserted and a hose clip applied. At the completion of the five minutes cycling, the tap leading into the Douglas Bag was opened, and the expired air collected for the five minutes immediately post exercise. Two Douglas Bags connected by a three - way tap were used, and expired air collected in one bag for the first ninety seconds, and collected in the other bag for the remaining three and a half minutes. During this five minutes post exercise period, the respirations per minute were counted. The whole proceedure was carried out in detail for four consecutive days prior to testing in order to familiarise the subject with the method.

The Douglas Bags were well shaken to ensure mixing of the expired air, and a sample of each bag was withdrawn through a Brodie Gas Sampler. Duplicate samples from each gas sampler were analysed in a Haldane Gas Analyser. These duplicate determinatives agreed within 0.04% for O_2 and 0.03% for CO_2. Frequent analyses were made on atmospheric air, checking 20.94 for the combined CO_2, and O_2 determinations within 0.03%. The mercury levelling bulb on the Haldane analyser had an automatic lowering and raising device run by a small motor.

For 20 subjects the complete test was repeated on three successive occasions to establish the reliability of the method. The intercorrelation of the three means gave a reliability for the O_2 consumption, $\gamma = 0.75$. These figures indicated that the reliability of repeated testing of the same subject with O_2 assays was sufficiently good to justify only one test being performed. This meant a great economy of time.



MEAN O_2 UPTAKE PER MINUTE FOR 5 MINS, POST (STANDARD) EXERCISE FOR 20 PATIENTS AND 20 NORMAL CONTROLS

FIG. III

Material —The subjects used for this study were the same as the first group tested for pulse response to standard work.

Results.

Oxygen Uptake After Standard Exercise. Fig 3

Figure 3 shows the O_2 uptake after exercise for the three groups, 20 normal controls, 10 E.S. patients and 10 anxiety states. The volumes represent the mean O_2 uptake per minute for the five minutes post exercise during which the expired air was collected in the Douglas Bags. Obviously the O_2 uptake during these five minutes is rapidly falling as the O_2 debt is repaid, but for comparative purposes the mean O_2 uptake per minute is the most convenient to use. Table 3 gives the same results in more detail. The volumes given for the normal controls are obtained from a single test, those from the patients are the mean of three tests done on successive days.

The mean O_2 uptake per minute for the 20 controls is 586 c,c, ± 35.9 s.d. (range 533 to 638). The mean of the ten E.S. patients is 729 ± 109.0 s.d. (range 581 to 923), and for the anxiety states 702 ± 126.0 s.d. (range 470 to 901). When the E.S. patients and anxiety states are added together, the mean O_2 uptake is 716 ± 118.2 s.d. (range 470 to 923).

The difference between the E.S. patients and the normal controls is significant (c.r. 3.83; $P < .01$), and probably significant for the difference between anxiety states and controls (c.r. 2.53; $P < .02$). The difference between E.S. patients plus anxiety states and controls is significant (c.r. 4.58; $P < .01$).

When the above group of 20 normal controls and 10 E.S. & 10 anxiety states was enlarged to include other groups of neurotics as described under pulse response to standard work, the following results were obtained.

TABLE 4

SIGNIFICANCE OF THE DIFFERENCE OF THE MEANS IN OXYGEN UPTAKE, BETWEEN THE NORMAL CONTROL GROUP AND 5 DIFFERENT GROUPS OF NEUROTIC PATIENTS, FOR 5 MINUTES IMMEDIATELY POST (STANDARD) EXERCISE.

	Oxygen Uptake c.c's. per min.	S.D.	C.R.	P.
20 normal controls	586	35.9		
12 E.S. Group 2	718	101.1	4.2	<.01
15 E.S. Group 3	673	70.5	4.2	<.01
10 somatic anxiety.....	703	126.0	2.7	<.02
12 hysterics	654	51.5	3.9	<.01
10 anxiety states	683	84.0	3.3	<.01
Total 59 neurotics.....	685	86.2	7.1	<.01

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Table 4.

Table 4 shows the mean oxygen uptake for the five minutes post exercise in the normal controls and five neurotic groups tested. It will be seen that all five groups of neurotics show a significantly greater oxygen uptake per minute than do the normal controls. The difference is most marked in Group 3 E.S. (c.r. 4.2; $P < .01$), and in the E.S. Group 2 (c.r. 4.2; $P < .01$), and least striking in the somatic anxiety group (c.r. 2.7; $P < .02$). The mean oxygen uptake for the 20 controls is 586 c.c. per minute $\pm$ 35.9 s.d., and for the total 59 neurotic patients 685 c.c. per minute $\pm$ 86.2 s.d.(c.r. 7.1).

3. Lactate Rise after Standard Work

Method.

Standard work on a bicycle ergometer was carried out as previously described. A sample of venous blood was removed for lactate determination.

(a) While the subject was resting and (b) 10 minutes after completion of the standard exercise.

The blood samples were analysed for lactate content; the ten minute sample representing the time when the lactate was probably at its peak. There is a l in the disappearance of lactate after exercise, which in the trained subject may last for six to eight minutes, but in the untrained or non-athletic subject may last two or three times as long (28).

The blood samples were drawn into tubes containing a small amount of mixture of potassium oxalate and sodium fluoride ground up together in the proportion of 1: 10. The latter was to prevent the lactic acid from decomposing. Determinations were made in duplicate following Friedmann's method (29). The treatment of the filtrate with $CuSO_4$ and $Ca(OH)_2$ was omitted as suggested for normal human blood (29). The oxidising agent used in the aeration procedure was N/10 $KMNO_4$. Acceptable determinations had blanks of not more than 0.1 c.c. of 0.002N. I_2 and the duplicates agreed within 0.05 c.c. of 0.002N. I_2.

TABLE 5

BLOOD LACTATE RISE ABOVE THE RESTING LEVEL FOLLOWING STANDARD WORK,

EXPRESSED IN MILLIGRAMMES PER CENT.

	Range	Mean	S.D.
20 normal controls	3 to 22	11.1	6.3
10 E. S. patients	8 to 35	21.4	8.6
10 anxiety states	0 to 27	15.9	7.8
10 E.S. and 10 anxiety states ...	0 to 35	18.6	8.4

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In testing the E.S. patients and the anxiety states, the complete test was repeated on three successive occasions to establish the reliability of the method. The intercorrelation of the three means for the lactate rise gave a reliability $y = 0.96$. These figures indicated that the reliability of repeated testing of the same subject with lactate assays was sufficiently good to justify only one test being performed.

Using the same 20 normal controls 10 E.S. and 10 anxiety states previously described under Pulse response and metabolic response to standard work the following results were obtained.

Results. Table 5 gives the blood lactate rise after exercise in the three groups --- controls, anxiety states and E.S. patients. The 20 controls gave a mean lactate rise of 11.1 mgm.% ± 6.3 s.d., and the 10 E.S. patients a mean lactate rise of 21.4 mgm.% ± 8.6 s.d., and the 10 anxiety states a mean lactate rise of 15.9 mgm.% ± 7.8 s.d., and the 10 E.S. patients plus 10 anxiety states a mean lactate rise of 18.6 mgm.% ± 8.4 s.d.

The difference between the controls and the E.S. patients (c.r. 3.12; $P < .01$), and the controls and E.S. patients plus anxiety states (c.r. 3.32; $P < .01$) is significant, but the comparison between the controls and the anxiety states is not significant (c.r. 1.64; $P < 0.1$). Of the 10 E.S. patients, 6 had a lactate rise greater than the highest control rise (22 mgm.%) while only one of the anxiety states showed a rise above this figure.

When the above groups are enlarged to include larger groups of neurotic patients the following results are obtained.

TABLE 6

SIGNIFICANCE OF THE DIFFERENCE OF THE MEANS IN LACTATE RISE, BETWEEN THE NORMAL CONTROL GROUP, AND 5 DIFFERENT GROUPS OF NEUROTIC PATIENTS FOR 5 MINUTES IMMEDIATELY POST (STANDARD) EXERCISE.

	Lactate Rise			
	Mgm.%	S.D.	C.R.	P.
20 normal controls	11.1	6.2		
12 E.S. Group 2	18.0	6.9	2.8	<.01
15 E.S. Group 3	19.9	8.8	3.1	<.01
10 somatic anxiety	15.8	7.8	1.6	<.1
12 hysterics	15.0	6.2	1.6	<.1
10 anxiety states	19.2	7.4	2.8	<.01
Total 59 neurotics	17.7	7.7	3.8	<.01

TABLE 7

VENTILATION RESPONSES FOR THE 5 MINUTES IMMEDIATELY FOLLOWING STANDARD WORK. BY OXYGEN EQUIVALENT IS MEANT THE AMOUNT OF VENTILATION REQUIRED FOR THE ASSIMILATION OF 100 C.C. OF OXYGEN

	Breaths per min.	Litres per min	O_2 uptake per min. c.c's	Oxygen Equivalent	O_2 uptake per breath c.c's	Volume per breath c.c's
20 controls...	18.3	17.0	586	2.901	34.1	929
10 E.S.patients .	30.6	30.5	729	4.184	26.0	996
10 anxiety - states ..	26.7	26.0	702	3.704	31.6	974
E.S. plus - anxiety states.	28.7	28.3	716	3.944	28.8	985

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Table 6

Table 6 shows the mean lactate rise following standard exercise. Both groups of E.S. show significant differences (E.S. Group 3, c.r. 3.1; $P < .01$, E.S. Group 2, c.r. 2.8; $P < .01$), and the anxiety states are also significantly different (c.r. 2.8; $P < .01$). The somatic anxiety states (c.r.1.6; $P < .1$) and the hysterics (c.r. 1.6; $P < .1$) do not appear to be significantly different from the normal controls. The mean lactate rise for the 20 controls is 11.1 mgm.% ± 6.2 s.d., and for the total 59 neurotic patients 17.7 mgm.% ± 17.1 (c.r. 3.8).

Table 7

4. Ventilation after Standard Work

Table 7 shows the essential factors regarding the post exercise ventilation in the patients and controls. It will be seen that for the five minutes post exercise, the mean respiratory rate per minute was 18.3 for the controls, 30.6 for the E.S. patients, and 26.7 for the anxiety states. The mean ventilation in litres per minute for the three groups was 17.0 L, 30.5 L, and 26.0 L respectively. As the mean oxygen uptake per minute for the three groups was 586 c.c., 729 c.c., and 702 c.c. respectively, the post exercise oxygen equivalent (i.e. the ventilation required for the assimilation of 100 c.c. of oxygen) was 2.9 for the controls, 4.2 for the E.S. patients, and 3.7 for the anxiety states. The oxygen uptake per breath was 34.1 c.c., 26.0 c.c., and 31.6 c.c. respectively for the three groups, and the volume per breath 929 c.c., 996 c.c., and 974 c.c. respectively in the controls, E.S. patients, and anxiety states.

TABLE 8

SIGNIFICANCE OF THE DIFFERENCE BETWEEN THE MEANS (C.R.) OF PULSE AREA, BLOOD LACTATE RISE, AND METABOLIC RESPONSE TO STANDARD WORK BY VARIOUS GROUPS OF NEUROTIC SUBJECTS, COMPARED WITH A CONTROL GROUP OF 20 NORMAL SUBJECTS.

	Pulse Area		Lactate Rise		O_2 Uptake	
	C.R.	P	C.R.	P	C.R.	P
12 E.S. Group 2	4.9	<.01	2.8	<.01	4.2	<.01
15 E.S. Group 3	3.3	<.01	3.1	<.01	4.2	<.01
10 Somatic anxiety	2.1	<.04	1.6	<.1	2.7	<.02
12 Hysterics	1.1	<.1	1.6	<.1	3.9	<.01
10 Chronic anxiety	5.8	<.01	2.8	<.01	3.3	<.01
Total 59 Neurotics	5.0	<.01	3.8	<.01	7.1	<.01

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Table 8

Discussion on the Response to Standard Work

From the results obtained (Table 8) it is clear that a significant differentiation between the exercise response of normal controls and E.S. patients (both Group 2 and Group 3) can be made in the three tests --- pulse area, O_2 uptake, and lactate rise. There is also a significant differentiation on all three tests between the controls and the chronic anxiety states who had no somatic anxiety symptoms, and made no complaint of poor exercise response. The difference between the controls and somatic anxiety states on the same three tests is probably significant, except in the case of the lactate rise --- (c.r. 1.64; $P < .1$). The somatic anxiety states had symptoms similar to those complained of by the E.S. patients, and apparently due to autonomic overactivity; the chronic anxiety states on the other hand, had no such symptoms although these had been present in the more acute stage of their illnesses; nevertheless the E.S. patients and chronic anxiety states showed poorer exercise response in our tests than did the somatic anxiety states. This suggests that autonomic overactivity alone was not responsible for poor exercise response. The group of hysterics approximated more to the control group, but the total group of 59 neurotics was sharply differentiated from the control group on all three tests.

Post exercise ventilation showed no evidence of deficient ventilation, the volume per breath was approximately equal in the controls, E.S. patients, and anxiety states, but in both groups of patients more ventilation was necessary for the assimilation of 100 c.c. of oxygen than in the controls. In other words the patients breathed less efficiently than the controls.

(b) MAXIMAL WORK

The bicycle ergometer as already described was used.

The procedure was similar to that adopted for the standard work experiments except that the subject was now asked to work to complete exhaustion, and an attempt was made to achieve this within ten minutes by choosing a suitable weight to start with, and if necessary adding further weights while the patient was actually pedalling. In view of the fact that no standard weight was used, no comparison of the amount of work done by the various subjects was possible. Actually, the E.S. patients, in the large majority of cases, reached their end point, within the ten minute period when doing work equivalent to 6,750 foot lbs. per minute; i.e.- the same work level as was used for the standard work. The controls invariably needed considerably more weight on the friction band.

It is fully realised that the "end point" must be an arbitrary one, dependent at least as much on psychological factors as on the physiological changes occuring as a result of physical work. All that can be said is that the conditions were standardised and every encouragement given to the subject to produce his best performance.

20 normal controls and 20 E.S. patients (8 Group 3 and 12 Group 2) were tested.

1. Pulse Response to Maximal Work.

The mean pulse rates for the resting pulse, the first four minutes after exercise, and the average of the eight to ten minutes period following maximal work, were as follows: controls, 70, 156, 131, 119, 113, and 104; patients, 71, 154, 134, 125, 119, and 106. Figure 4 shows how closely the pulse curve of the controls and patients now correspond.

2. Blood Lactate Rise following Maximal Work

As in the standard work, a blood sample for lactate estimation was removed at rest, and ten minutes after the cessation of exercise.

In the 20 controls the mean lactate rise was 78.0 mgm. ± 16.3 s.d. (the

mean resting value was 11.2 mgm.% ± 2.79 s.d., and the mean maximal figure was 89.2 mgm.% ± 17.01 s.d.).

The 20 E.S. patients gave a mean rise of lactate from the resting level 50.2 mgm.% ± 11.06 s.d. (mean resting level 12.6 mgm.% ± 3.1 s.d., and mean maximal figure 62.8 mgm.% ± 11.28 s.d.). The significance of the difference between the means (c.r.) is significant, the difference being 6.22 ($P < .01$).

Of these 20 patients, 8 belonged to Group 3 E.S., and 12 to Group 2 E.S. Both groups gave almost similar results, the mean maximal lactate rise being 48.0 mgm.% in Group 3 and 51.1 mgm.% in Group 2.

3. Blood Gas Analysis and Ph ~~Material and Technique~~.

Material and Technique

A group of 10 Group 2 E.S. patients was chosen, all of whom were free from organic disease and had ages ranging from 25 to 31. They all gave a history of effort intolerance from earliest recollection, and it was felt that constitutional physical inferiority was more important in these men, and had more to do with their excessive response to exertion than had emotional factors.

A group of 16 controls was taken from the available hospital staff, and included seven doctors, none of whom took any regular exercise, four members of the physical training staff, and five others of whom two did a certain amount of track running.

Blood samples were taken from the subject at rest, immediately after the cessation of exercise, to give the pH and lactate picture at the exhaustion point, and a third sample 5 to 10 minutes later, to give the maximum lactate figure, and also to determine the behaviour of carbon dioxide during recovery. The first and third samples were arterial blood taken from the femoral artery of each leg. The second sample was arterialised venous blood from the median basilic vein of the arm which had been heated to 45° C. in an arm-bath; this was done in preference to arterial puncture because the blood sample could be

TABLE IX

Changes in the arterial blood chemistry of 10 E.S. patients worked to exhaustion point on a bicycle ergometer. The figures in the TIME column represent resting, the time worked before exhaustion, and the time interval between the completion of exercise and the removal of the third blood sample (in minutes).

CASE	TIME	O_2 C.P.	O_2 Sat.	pH	Shift	pCO_2	$BHCO_3$	LACTATE	INCREASE
1.	0.0	20.1	97	7.42		40	24.2	8.0	
	3.1	21.8	94	7.31	.11	42	20.1	38.2	34.8
	7.3	21.2	96	7.36		31	17.0	42.8	
2.	0.0	22.2	97	7.45		35	22.8	8.1	
	4.0	23.1	93	7.38	.07	39	21.6	19.6	28.0
	7.0	22.4	98	7.40		35	20.3	36.1	
3.	0.0	19.4	97	7.43		40	24.7	14.7	
	4.3	20.2	91	7.39	.04	36	20.2	35.8	22.3
	10.0	19.7	96	7.44		33	21.4	37.0	
4.	0.0	21.0	96	7.41		39	23.2	22.6	
	4.5	22.4	95	7.34	.07	39	20.0	55.2	32.6
	10.0	21.2	95	7.39		38	21.4	47.3	
5.	0.0	20.1	93	7.44		39	21.4	11.3	
	5.0	21.1	92	7.34	.10	39	25.1	31.6	20.3
	5.0	20.6	93	7.44		33	19.7	26.9	
6.	0.0	20.0	96	7.43		38	21.2	6.4	
	5.4	21.6	72	7.32	.11	43	23.0	24.4	28.4
	5.0	20.4	96	7.37		28	20.5	34.8	
7.	0.0	17.6	97	7.44		38	15.7	9.1	
	6.2	18.7	92	7.36	.08	36	24.0	52.1	43.0
	6.5	18.5	95	7.40		34	19.2	39.0	
8.	0.0	21.5	95	7.44		40	20.2	9.1	
	6.5	22.6	95	7.36	.08	37	25.7	43.4	34.3
	7.2	21.8	97	7.40		34	19.5	43.4	
9.	0.0	19.4	97	7.43		41	20.0	17.5	
	7.0	21.5	92	7.32	.11	37	25.6	89.0	71.5
	10.0	20.2	97	7.34		43	18.0	90.7	
10.	0.0	20.3	92	7.41		39	23.6	8.3	
	7.1	22.0	100	7.30	.11	31	14.9	55.4	47.1
	6.0	20.4	98	7.32		33	16.7	44.3	

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obtained without the slightest delay. Arterial punctures were not used in the controls as the physiology of exercise in normal people and in athletes has been extensively studied elsewhere, and the results would not affect the conclusions to be drawn about E.S. The blood, having been withdrawn in an all-glass syringe lubricated by the minimum amount of paraffin was transferred under oil to a centrifuge tube and cooled in ice-water immediately. Samples were analysed for: oxygen capacity by the method of Sendroy (Peters and Van Slyke (30): oxygen content and carbon dioxide content (Peters and Van Slyke (30): pH (Barker and Summerson (31).

Table 9

Results

Oxygen Metabolism.

Table 9 gives the figures for oxygen combining power and oxygen saturation of arterial blood before, immediately following and approximately 5 to 10 minutes after maximal work in 10 Group 2 E.S. patients. It is immediately apparent that there is no evidence of anoxaemia in the resting blood or even post exercise. Case 6 is the only exception (oxygen saturation immediately after exercise 72%); all other bloods taken post exercise have an oxygen saturation of 91% or over.

Hyperventilation

Table 9 gives the results obtained from maximal work in the 10 E.S. patients tested. It will be seen that there is no evidence of respiratory alkalosis resulting from resting or post exercise hyperventilation.

The results show clearly that though there may be a fall of carbon dioxide pressure after exercise, this is not abnormal in amount (generally 3 or 4 mm.Hg, the most extreme being a fall from 38 to 28 mm. Hg.) and is correlated with fall of bicarbonate following the production of lactic acid. In no case did the blood pH become more alkaline than the resting value.

It might be argued that we have looked for the development of alkalosis too soon. We were guided by the fact that in all the patients chosen,

excessive respiration had almost died away 5 min. after the conclusion of exercise, and whenever we have taken another blood sample after a further 5 min. this has simply shown a slow return of the pH to the resting value.

Blood Lactate Rise.

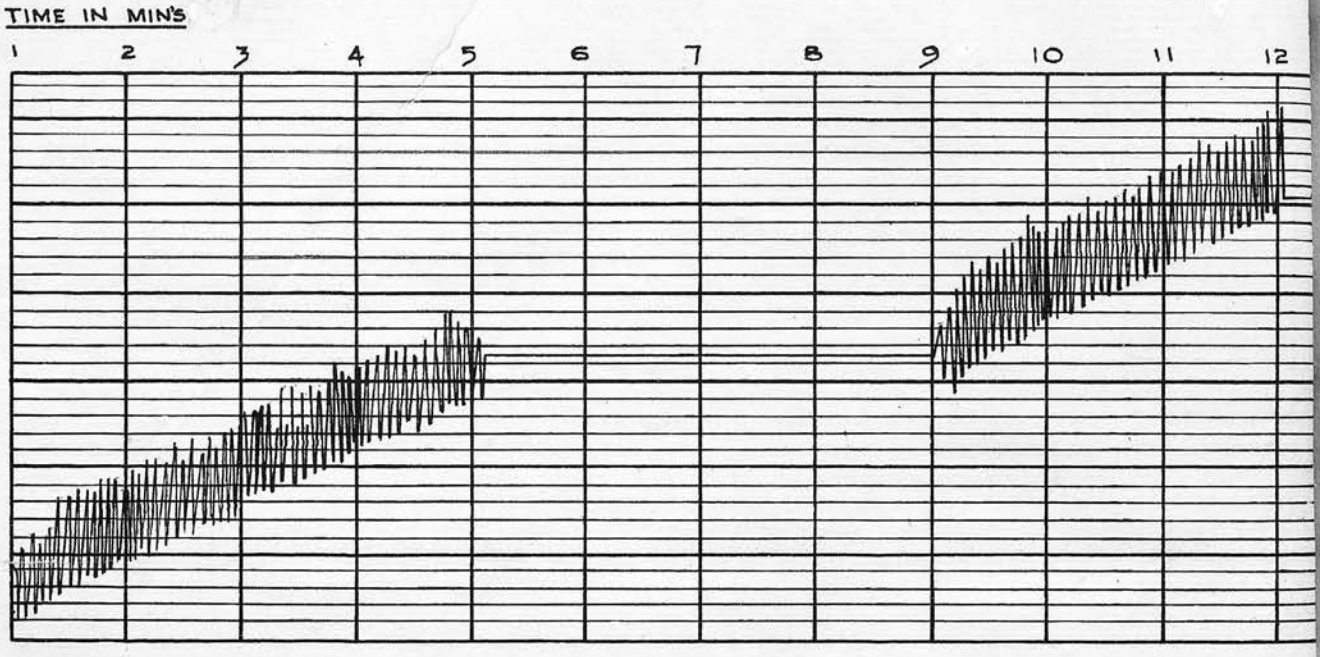
Table 9 includes resting and post exercise blood lactate levels as they afford a good index of the physiological state of the patient when he reached 'exhaustion point'. These patients show an even lower lactate rise than the 20 E.S. patients already described (see page 22); a mean rise of 36.2 mgm.% compared with 50.2 mgm.%.

Discussion on Response to Maximal Work.

In considering the response to maximal work, it is clear that the lactate rise when the 20 E.S. patients exercised to complete exhaustion on the bicycle ergometer (mean rise 50.2 mgm.% ± 5.74 s.d.) was significantly different from the response of the 20 controls (mean lactate rise 78.0 mgm.% ± 8.15 s.d.). There was no real difference between Group 2 and Group 3 E.S. in this respect. Kuehr, Dill and Neufeld (25) have shown that, in running, the ordinary young man will stop from exhaustion when the lactate level in the blood has reached approximately 100 mgm.% (i.e. lactate rise of about 90 mgm.% above the resting level). As more muscles are employed in running than in the type of ergometer we used, our lactate control figures are understandably somewhat lower than those of the Harvard Group. The results obtained suggest that E.S. patients (both Groups 2 and 3) give up exhausting physical work before they have reached a "physiological" end point. The fact that these patients typically dread the supposed ill effects of strenuous physical exercise, because they fear the damage which may result to their hearts etc., results in what amounts to an effort phobia.

The arterial blood gas analysis gave no evidence of anoxaemia; at rest

the Oxygen saturation of arterial blood in 10 E.S. patients ranged from 97% to 92% (mean 95.6%), and after maximal work the oxygen saturation was found to be below 90% in only one case. The suggestion put forward by Haldane et al (19), and later by Hick et al (24) that the symptoms of effort syndrome were due to anoxaemia of effort, was contraindicated by our findings. Nor did we find any evidence to support the hypothesis of Soley and Shock (23) that E.S. is the result of respiratory alkolosis. After maximal work no E.S. patients showed evidence of hyperventilation alkalosis --- the blood pH was never found to become more alkaline than the resting value, and the carbon dioxide pressure fell by only 3 to 4 mm. Hg. in most cases the greatest fall being 10 mm. Hg.



— FIG; 5. —

— RESPIRATORY EXCERCISE TOLERANCE TEST. —

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(c) LIGHT WORK

Metabolic response to light work or Respiratory exercise tolerance test.

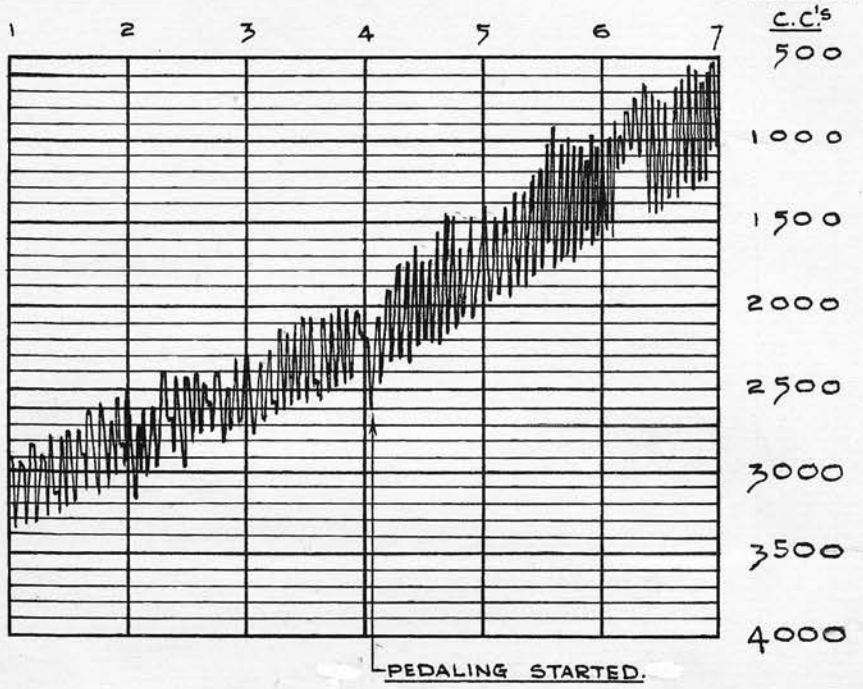
Fig 5

Method.

A portable Benedict metabolism apparatus was used, and on the day previous to a test the patient was familarised with the procedure. The exercise was performed on a bicycle ergometer. When tested the subject rested comfortably on the couch for half an hour, after which the mouthpiece of the spirometer was put in position, and a kymograph record of the respirations made for four to five minutes(see Fig. 5). The tap was then turned so that the subject was breathing from the outside air. He now placed his feet on the pedals and pedalled at forty-two revolutions per minute for exactly one minute, the friction of the brake band being equivalent to a weight of 6 pounds (~~3 Kg.~~), i.e., 4,500 ft. lbs. per minute. He then lay recovering his breath for a further three minutes, at the end of which time the tap was again turned on, and the respirations for the fourth, the fifth and the sixth minute after exercise recorded. The mean minute volume before and after exercise was then compared, the latter being expressed as a percentage of the former.

Results.

We have figures of 10 controls and 13 E.S. patients. The mean for the controls was 107 per cent $\pm$ 10.4 s.d.; i.e., the ventilation in the period four to six minutes after exercise was 7 per cent greater than the resting ventilation, while the mean for the patients was 134 per cent $\pm$ 14.2 s.d. The difference between the two means is significant (c.r. 5.0; $P < .01$), and the ranges are such that the test probably has diagnostic value within certain limits.



— FIG. 6. —

— PEDALING UNOPPOSED — NORMAL RESPONSE. —

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(d) MINIMAL WORK OR PEDALING UNOPPOSED

Method.

Pedaling Unopposed.

Spirometric tests are of value only when breathing is reasonably regular, when a patient's co-operation can be obtained and when the patient is not emotionally upset by the procedure. Some patients may breathe well at rest, but when they are put in a work situation anomalies of breathing occur. In order to categorise the good and the bad breathers, and in order to observe the effect of a work situation on respiration we make use of the following procedure: A subject lies on his back and breathes into the spirometer for five minutes at rest; he is then asked to place his feet on the pedals of the bicycle ergometer and pedal slowly for seven minutes. As the brake band is not in use, the subject pedals against no resistance; there is normally little increase in the total ventilation or oxygen uptake. (see Fig.6)

Results.

Of 75 E.S. patients tested, 36 or 48 per cent gave a normal tracing: 25 or 33.3 per cent showed ventilation in excess of normal, and of these, although only 1 patient gave clinical signs of tetany, practically all the remaining patients complained of giddiness, headache, breathlessness, tiredness in the legs or pounding of the heart; parathesias were not complained of. Six patients (8 per cent) gave up before the end of the seven minutes saying they were exhausted. Of these, 2 had symptoms and signs indicating tetany; 1 appeared to lose consciousness, although there were no other tetanic manifestations, and of the remaining 3, 2 showed hyperventilation but no tetany and 1 showed a progressive decrease in the volume per breath to such an extent that anoxaemia probably contributed to his breakdown. The remaining 8 patients (10.7 per cent) gave tracings with irregular breathing and were all mostly persons who were emotionally upset by the test. Thus, of the 75 patients tested,

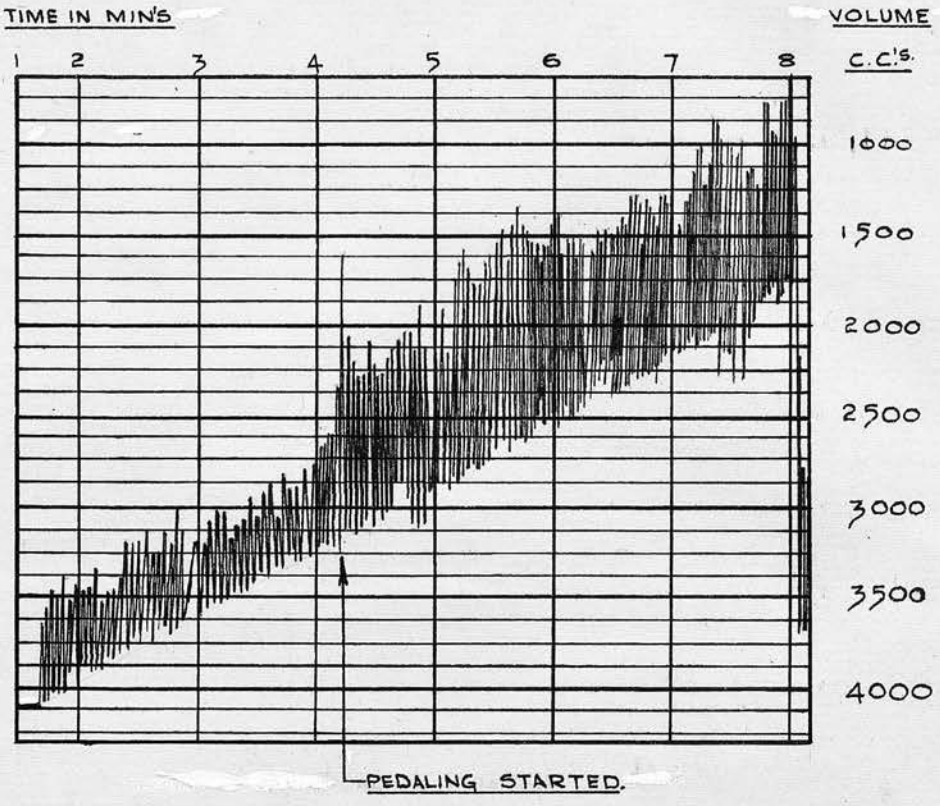

FIG. 7.

PEDALING UNOPPOSED — HYPERNOEIC RESPONSE.

type

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only 48 per cent appeared to breathe normally in a work situation.

These results show the neurotic trends of many of the subjects tested and the tendency for irregular and excessive breathing to occur in a work situation, although practically no work is performed by the subject.(see Fig.7)

DISCUSSION OF THE RESULTS ON EXERCISE RESPONSE.

The Standard work test differentiates significantly between groups of normal controls, and both Group 2 and Group 3 E.S. patients, and chronic anxiety states, when any of the 3 criteria -- pulse response, oxygen uptake, or blood lactate rise --- is used. The same is probably true when we compare groups of normal controls and somatic anxiety states. Hysterical patients as a group cannot be differentiated from normal controls in this way. While it is true that the above groups of neurotic patients can be differentiated from normal controls by the tests mentioned, it is doubtful if the application of these tests to the recovery period following moderate work is the best available proceedure. Craig Taylor (33) has shown that the individuals fitness for hard work is best measured during exercise, and not during the recovery phase. On maximal work he finds that the time run is more reliable than any of the physiological measures he used (heart and respiration rates, ventilation, blood lactate, and oxygen consumption). Heart rate and blood lactate were the most reliable submaximal measures , but are approximated in maximal work by per cent oxygen and oxygen consumption. Unfortunately, because of the feeling of suffocation and other emotional difficulties, which inevitably occur when testing neurotic subjects we were forced to apply our tests only during the post exercise recovery period.

The ventilation response to standard work shows clearly that comparing

groups of normal controls, and E.S. patients, and somatic anxiety states, the patients breathe much more rapidly following exercise although the volume per breath is much the same in all three groups. Obviously, the patients hyperventilate compared with the controls, but the blood gas studies following maximal work show no evidence of respiratory alkalosis. The respiration of the two groups of patients appears to be less efficient than in the control group --- the relatively low oxygen equivalent (ventilation required for the assimilation of 100 c.c. of oxygen) in the control group is one way of expressing this greater efficiency.

The lactate rise following maximal work was significantly different between controls and E.S. patients (both Groups 2 & 3). This difference would appear to be due to the effort syndrome's 'effort phobia' - i.e.- his unwillingness (probably often unconscious) to overtax his strength for fear of damaging his heart etc. Unfortunately we had to use an improvised bicycle ergometer so that the amount of work done before exhaustion could not be measured. We did not test other groups of neurotics on maximal work so cannot say if the relatively small lactate rise following 'maximal' work is an attribute of neuroses in general.

Using a respiratory exercise tolerance test (a measure of the ventilation response to light work), we found it possible to differentiate a group of normal controls from a group of E.S. patients.

Of the three responses to standard work, which were tested --- pulse rise, lactate rise, and oxygen uptake --- oxygen uptake seemed to be the most satisfactpry test for differentiating normal controls and the various neurotic groups. All groups of neurotic patients were significantly different from the controls ($P < .01$) except the somatic anxiety group which was probably significant ($P < .02$). For the total group of 59 neurotics tested compared with the group

of 20 normal controls the significance of the difference between the means for the 3 tests was; oxygen uptake-c.r.7.1 ; pulse area-c.r.5.0 ; lactate rise-c.r.3.8.

No conclusions can be drawn as to the cause of the poor exercise response in patients complaining of symptoms of effort intolerance --- clinically E.S. Groups 2 & 3. The nature of the response to maximal work indicates that there is an 'effort phobia', but this does not explain the relatively inefficient pulse, lactate, and oxygen uptake response in E.S. patients compared with controls. The fear of possible ill effects of heavy work in the E.S. patients, presumably produced a state of muscle tension, and as was shown in our pedaling unopposed studies, marked anomalies of respiratory pattern were often produced by the mere work situation, even though no significant amount of work was performed. Hyperventilation often occurred on exercise but without the production of respiratory alkalosis. This hyperventilation represented excessive work by the muscles of respiration, and might possibly contribute to the inefficient performance. A normal control with a mean oxygen uptake of 555 c.c. per min. for the 5 mins. post standard exercise repeated the standard work simulating the hyperventilation of the E.S. subject; he breathed at 42 respirations per min. during the exercise, and 60 per min. post exercise; the mean oxygen uptake was now 606 c.c. per min. while the lactate rise showed no difference (7.0 mgm.%); post exercise ventilation had been increased from a mean of 19.4 litres per min. to 30.4 litres per min: breathing in this manner proved to be hard work and was difficult to maintain; there were no symptoms or signs of hyperventilation tetany. The same subject was given intravenous atropine gr. 1/100 at a time, until no further pulse rise occurred; the pulse rate rose from 69 to 138/at which point the standard exercise was started; for this test per min. the mean oxygen uptake for the 5 mins. post exercise was 900 c.c. per min., and

the lactate rise 14.0 mgm.%; the mean post exercise ventilation was 26.5 litres per min. Subjectively the control complained of dry mouth, postural giddiness, muscular inco-ordination on walking, fatigue, irritability, diminished pressure on micturition, feeling of eye strain and difficulty in accomodation. Finally, the same subject was given 0.7 c.c. of 1;1000 adrenalin solution subcutaneously: after 10 mins. a tense feeling in the epigastrium, mild palpitation, and a feeling of constriction in the chest were remarked, and there was pallor of the face --- the pulse had risen from 64 to 81, and at this point the standard exercise was started. Unlike the atropin test no difficulty was experienced during the pedaling, and no subjective discomfort was described post exercise. The mean oxygen uptake for the 5 mins. post exercise was 538 c.c. per min. These results suggest the possibility of changes in exercise efficiency in relation to functional changes in the involuntary nervous system; however consideration of the clinical material used does not clarify the situation very much. Symptoms and signs due to vegetative dysfunction.were present in E.S. Group 2, E.S. Group 3, and somatic anxiety states, and were absent in the chronic anxiety states and hysterics. If clinical evidence of disturbance of vegetative function (~~[illegible]~~) were the determining factor in exercise efficiency then both the chronic anxiety and hysterical groups would perform as efficiently as the normal control group: this did not prove to be the case and the chronic anxiety group was significantly different from the control group on all three tests on standard work --- pulse, lactate,and oxygen uptake --- while the hysterical group was significantly different from the control group in oxygen uptake.

We sought other physiological leads which might throw some light on the mechanism if not the aetiology of poor exercise response. The forearm blood flow was measured with a Lewis & Grant plethysmograph. We measured the arm

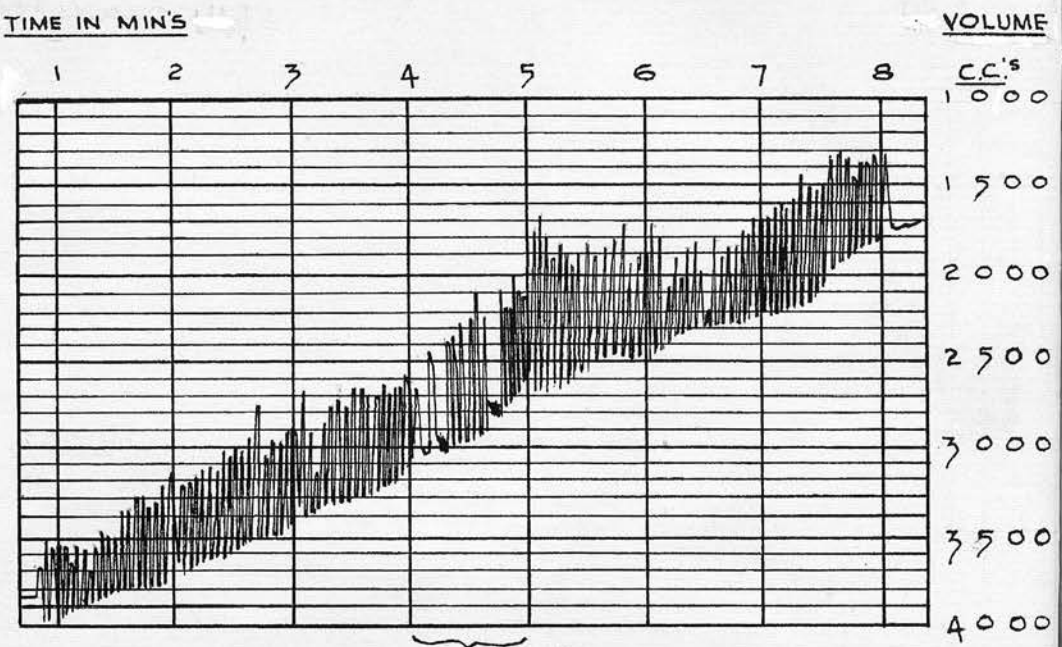
blood flow at rest and then following work on the bicycle ergometer; to our surprise no increase in the arm volume occurred until very heavy work was done --- apparently the increased blood flow caused by the work, was all directed to the leg muscles which were doing the work; certainly it did not reach the arms, until the subject was near exhaustion. This 'homeostasis' was less marked in the E.S. patients than in the controls; in fact some controls even when worked to complete exhaustion showed no rise in the arm blood flow. We gave up this promising line of enquiry because we had no facilities to control environmental circumstances (temperature humidity etc.) and test\restest reliability proved unsatisfactory.

Studies of cardiac output following work, by the direct Fick method (McMichael & Sharpey - Schafer (34)) were contemplated, but permission to catheterise the right auricle in service patients was refused.

By applying a tourniquet to the upper arm, and eliminating the general circulation we hoped to study the local muscle chemistry, particularly the lactate rise following a known amount of work to the forearm muscles, but removing constant amounts of venous blood proved difficult and again we could not/ obtain a high day to day reliability.

In brief our efforts to measure poor exercise response in E.S., met with some degree of success, but no real understanding of the mechanism of this poor exercise response was achieved.

Having studied the neurotics response to exercise stress, we decided to apply other stresses, and see if again differences between groups of normal controls and neurotics could be demonstrated.



— FIG; 8. —

— VENTILATION RESPONSE TO A PAINFUL STIMULUS. —

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2. RESPONSE TO PAIN

For this test we measured the ventilation and blood pressure response to a painful stimulus applied for approximately 2 mins. The choice of a suitable painful stimulus presented difficulties as we wished to use a relatively long test period. We finally decided to ask the patient to squeeze a rubber bulb 'till empty of air at a rate of 80 squeezes per min. (timed by a metronome). Immediately before starting this work a sphygmomanometer cuff was applied to the upper arm and the circulation to the limb cut off by applying a pressure of 200 mm. Hg. The ischaemia was maintained for 2 mins. in all --- one min. while pumping and one min. afterwards. During this time, a dull ache of increasing intensity was experienced by the subject.

Material

20 normal controls (a random sample of young soldiers), 10 cases of E.S., and 10 cases of somatic anxiety not complaining of effort intolerance, and eight cases of conversion hysteria were used for these tests.

(a) Ventilation

The subject lay comfortably on a couch, and was habituated to the use of the portable Benedict metabolism apparatus. On the day of the test he was not fasted but rested for 30 mins. on the couch before the test was started. When 3 mins. regular breathing had been recorded on the spirogram the arm circulation was cut off, and simultaneously the subject started squeezing the bulb. The subject continued to breathe through the closed circuit and respirations were recorded for 3 mins. following the cessation of pumping - i.e. 1 min. with the arm circulation still cut off, and two mins. with the circulation restored (see Fig. 8). The spirogram was then examined, and the average ventilation per min. for the 3 mins. at rest calculated. The

TABLE 10

VENTILATION RESPONSE TO A PAINFUL STIMULUS. UNITS REPRESENT PERCENTAGE RISE OR FALL OF VENTILATION COMPARED WITH THE RESTING VENTILATION (MEAN OF 2 TESTS CARRIED OUT ON SUCCESSIVE DAYS.)

	Range of Ventilation	Mean incr.% Ventilation	S.D.	C.R.	P
20 Normal controls...	-11 to + 72	10.4	16.5		
10 E.S. patients	- 3 to + 90	36.2	32.0	2.5	<.02
10 Anxiety states ...	-13 to +148	43.0	51.9	1.95	<.04
10 E.S. and 10 anxiety states	-13 to +148	39.6	43.4	2.9	<.01
8 Hysterics.....	+5 to +140	57.1	42.7	3.0	<.01

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ventilation during the minute when the subject was pumping was ignored but the ventilation for the next minute - i.e. when the pain stimulus was at its maximum, was measured (see Figure 8). This result was now expressed as a percentage rise or fall compared with the resting figure. The test was repeated on two successive days, and the final figure represented the mean of these 2 tests.

Table 10

Results

Table 10 shows the ventilation response to pain in the 4 Groups studied. In 20 normal controls the ventilation showed a mean increase per cent of 10.4 ± 16.5 s.d. (Range -11 to + 72). Four subjects showed a decreased ventilation as a result of the pain stimulus. The 10 E.S. patients gave a mean % ventilation increase of 36.2 ± 32.0 s.d. (Range -3 to + 90) ... (c.r. 2.5; P < .02). The 10 anxiety states gave a mean % ventilation increase of 43.0 ± 51.9 s.d. (Range - 13 to + 148) ... (c.r. 1.95; P < .04). Taking the anxiety states and the E.S. patients together as a group of 20 patients the mean % ventilation increase is 39.6 ± 43.4 s.d. (c.r. 2.9; P < .01). The group of 8 hysterics also differs significantly from the control group; mean % ventilation increase 57.1 ± 42.7 s.d. (c.r. 3.0: P < .01).

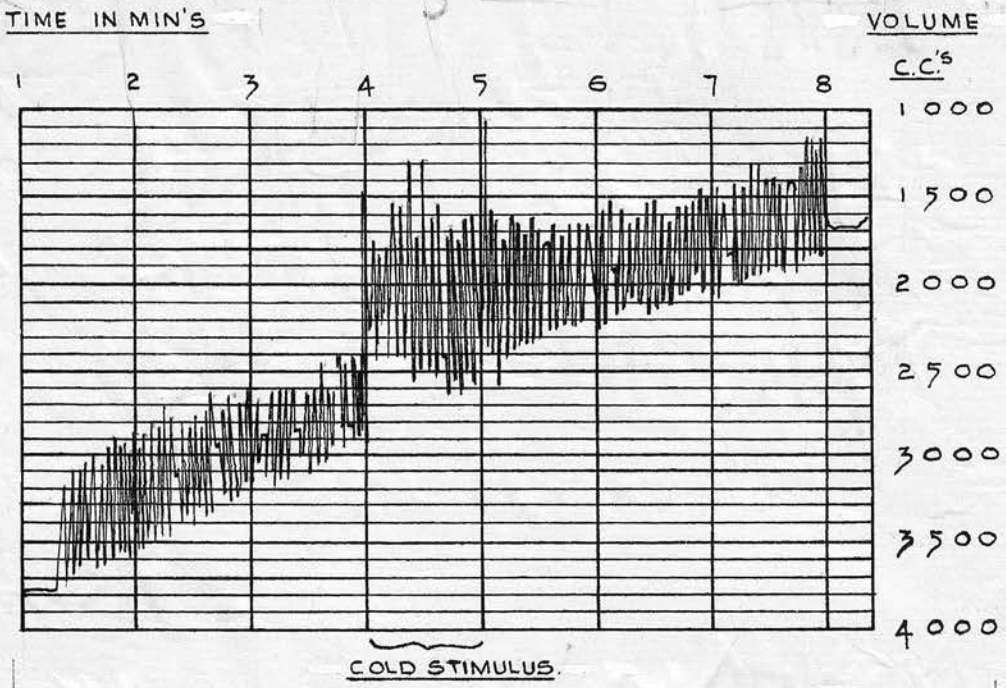
(b) Blood Pressure Responses.

The same groups of patients and controls were used as in the last test, except that 2 hysterics were added bringing the total of this group up to 10. The subject was rested lying down for 20 - 30 mins. with a sphgmomanometer cuff on both upper arms. When the B.P. was constant the circulation of the arm was cut off, and the subject squeezed a bulb for 1 min. in the manner already described. During the second minute when the ischaemic pain was increasing two B.P. readings were taken, and then minute readings for the next five mins. The first two readings were invariably higher than the succeeding readings, and the higher of these two (systolic and diastolic) was used for comparison with

the resting B.P. As before each test was repeated on two successive days and the mean of the results calculated.

Results

All but 2 (both controls) of the 48 subjects tested, showed a rise of systolic B.P. during the ischaemic pain. No signficant differences were found between the various groups. Controls mean rise of systolic and diastolic B.P. 14/16 mm.Hg. (Range of systolic B.P. - 3 to + 34 mm. Hg.) Parallel figures for the other groups were 10 E.S. patients 11/11 mm. Hg (Range 3 to 25 mm. Hg.), 10 anxiety states 10/10 mm. Hg.(Range 2 to 21 mm. Hg), 8 Hysterics 13/18 mm. Hg. (Range 3 to 24 mm. Hg.)



—FIG. 9.—

—VENTILATION RESPONSE TO A COLD STIMULUS.—

TABLE 11

VENTILATION RESPONSE TO COLD UNITS REPRESENT PERCENTAGE RISE OR FALL OF VENTILATION COMPARED WITH THE RESTING VENTILATION.

(Mean of two tests carried out on successive days)

	Range of Ventilation	Mean incr./ Ventilation	S.D.	C.R.	P.
20 normal controls ...	-8 to +27	8.1	9.5		
10 E.S. patients..	-6 to +91	32.3	25.2	2.9	<.01
10 anxiety states.	-13 " +72	31.1	23.7	2.9	<.01
10 E.S. and 10 anxiety	-13 " +91	31.5	25.8	3.7	<.01
8. hysterics ...	-6 " +77	27.0	22.1	2.4	<.03

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9.

3. RESPONSE TO COLD

The procedure in these tests was similar to that used for the ischaemic pain test except that a cold stimulus was substituted for the painful stimulus. The same 48 subjects were used as in the previous test. The technique for B.P. response was identical with the cold pressor test described by Hines (32).

(a) Ventilation

The patient breathed into the closed circuit of a Benedict metabolism apparatus as before. After a satisfactory resting ventilation had been recorded for three minutes, the forearm and hand was immersed in a bath of water at 3°C, and held there for 1 minute. Respirations were recorded during this minute and for three further minutes, after the arm had been withdrawn from the water. (see Fig. 9) The average ventilation per minute for the 3 minutes at rest was compared with the ventilation for the minute during the cold stimulus and the rise or fall expressed as a percentage of the resting ventilation. As before each test was repeated on two successive days, and the mean percentage rise or fall taken.

Table 11

Results.

Table 11 shows the ventilation response to cold in four groups studied. The 20 normal controls showed a mean increase per cent of 8.1 ± 9.5 s.d. (Range -8 to + 27). Three subjects gave negative results.

The 10 E.S. patients gave a mean % ventilation increase of 32.3 ± 25.2 s.d. (Range -6 to + 91) ... (c.r. 2.9; $P < .01$). The 10 anxiety states gave a mean % ventilation increase of 31.1 ± 23.7 s.d. (Range - 13 to + 72) ... (c.r. 2.9: $P < .01$). The group of 20 E.S. and anxiety states gave a mean % ventilation increase of 31.3 ± 25.8 s.d....(c.r. 3.73; $P < 0.01$). The eight hysterics showed a mean % ventilation increase of 27.0 ± 22.1 s.d. (Range -6 to +77)... (c.r. 2.4; $P < .03$)

(b) Blood Pressure Response.

The same subjects were used as in the previous tests. When the resting B.P. had become constant the hand and forearms were immersed in a bath of water at 3°C for 1 minute. Two B.P. readings were taken during this minute, and then one reading for the next 5 mins. The highest reading was compared with the resting B.P. The test was repeated on two consecutive days and the mean rise or fall of systolic and diastolic B.P. recorded.

Results

One hysteric and one anxiety state showed no rise of systolic B.P. otherwise all 48 subjects showed a rise. No significant differences were shown between the various groups. The controls showed a mean rise of systolic and diastolic B.P. of 7/11 mm. Hg. (Range of systolic B.P. 0 to + 18 mm. Hg.). Parallel figures for the other groups were 10 E.S. patients 11/11 mm. Hg. (Range -4 to + 23 mm. Hg.), 10 anxiety states 7/9 mm. Hg. (Range 0 to 10 mm. Hg.), 8 hysterics 8/11 mm. Hg. (Range 0 to + 15 mm. Hg.).

DISCUSSION ON RESPONSE TO PAIN AND COLD

The response to pain and cold stimuli may be discussed together, because the same subjects were used for both tests and the results are very similar in the 2 tests.

Comparison between the normal controls and neurotic subjects shows that the 2 Groups are clearly differentiated by the respiratory response to pain and cold, but cannot be differentiated by the B.P. response to these two stimuli.

The ventilation response to cold (Table 11) differentiates the controls and neurotics rather better than does the response to pain (Table 10). The ventilation response to cold is significantly different ($P. < .01$) between the controls and the E.S. and anxiety groups, and probably significant ($P. < .03$) with

the hysterics.

The ventilation response to pain is significantly different ($P < .01$) between the controls and hysterical groups, and probably significant with the E.S. ($P < .02$) and anxiety groups ($P < .04$).

Taking the total 28 neurotic subjects and comparing them as a group with the 20 controls, the ventilation response to both pain and cold is significantly different between the two groups.

Test retest reliability.

The total 48 subjects used in the ventilation response to both pain and cold were given each test on two separate occasions; only a fair degree of reliability is shown by the two tests by applying the method of product moment correlation; for the pain response $y = 0.625$, and for the cold response $y = 0.506$.

The B.P. response to both pain and cold failed to show any significant difference between the control and neurotic groups. Studying the cold response Hines (32) in his cold pressor test, considers a systolic rise of 14 mm. Hg, and a diastolic rise of 10 mm. Hg. as indicating incipient hypertension; 4 controls showed a systolic rise of more than 14 mm. Hg. on one test only; 3 E.S. patients showed such a rise on both tests, and 1 E.S. patient on one test only; 3 anxiety states showed such a rise on one test only; 1 hysteric showed the response on both tests, and 2 on only one test. Hines found a positive response in 15% of his controls; if one positive test is accepted (and it is not demanded that the test be positive on both testings) then we found the test positive in controls 20%, E.S. 40%, anxiety states 30%, and hysterics 30%.

TABLE 12

	First Interview			Basal			Difference		
	P	R	BP	P	R	BP	P	R	BP
10 E.S. patients	84	22	144/85	70	19	114/72	14	3	30/13
10 Anxiety States	81	23	138/79	65	20	113/74	16	3	25/5
10 Hysterics	72	19	132/82	69	19	115/75	3	0	17/7

Mean pulse respiration & blood pressure readings for 3 groups of patients at first interview (when excited), and 2 - 3 weeks later under basal conditions. (Pulse and respirations per min.)

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4. RESPONSE TO EXCITEMENT

It is difficult to devise an anxiety producing situation which represents a suitable standard stimulus. We considered using the air raids on London, but although these certainly produced fear responses there was no hope of standardising the test situation. We finally decided to take the patient within a few minutes of his admission to the ward, and in the strange company and environment of the doctor's Office. The patient was simply asked to remove his jacket and lie down; his pulse and respirations were recorded and B.P. was then measured. Two to three weeks later the patient was kept in bed fasting, and the above measurements repeated.

Material.

Unfortunately it was impracticable to use the above proceedure on normal controls as their relationship to the Dr. would have been different compared with the patients, and they were not living in hospital, and therefore not becoming familiarised with the hospital surroundings. Despite the lack of normal controls for comparison with the patients it was felt that the test should be carried out on patients; 10 E.S. patients, 10 anxiety states, and 10 patients with conversion hysteria were studied.

Results. Table 12

Table 12 shows the mean figures of pulse, respirations and B.P. at the first interview (when excited), and some weeks later (when relaxed), for the three groups of patients tested. All three groups show a drop in the readings under basal conditions compared with the first interview --- this drop is less marked in the hysterical group than in the other two groups, but there is no significant difference between the groups.

Taking the 10 E.S. & 10 anxiety states together the mean figures are as follows.

	Pulse	S.D.	Resp.	S.D.	Syst B.P.	S.D.
First interview...	82	15.8	22	4.7	141	10.3
Basal	67	10.3	19	4.6	114	14.6

If one compares the mean systolic B.P. at first interview (141), with the mean basal systolic B.P. (114) in this group, the difference is significant (c.r. 6.8; P < .01). The drop in mean pulse between the two interviews is also significant (c.r. 3.6; P < .01). The fall in respirations is probably significant (c.r. 2.0; P < .03).

Under basal conditions the systolic B.P. was below 100 mm. Hg. in 1 E.S. patient, in 3 anxiety states, and in 1 hysteric.

10.

Discussion on Response to Excitement

The results obtained show how misleading pulse, B.P., and respiration measurements may be in neurotics unless allowance be made for the emotional factor. Unfortunately, as no normal controls were available, it cannot be said that the results furnish further evidence of the relative vegetative overresponsiveness in neurotics indicated by the results of previous tests.

TABLE 13

	BREATHHOLDING			LEG RAISING		
	Mean (secs)	S.D.	C.R.	Mean (secs)	S.D.	C.R.
20 Normal Controls.	57.0	21.2		312	147	
50 Patients (35 E.S. & 15 anxiety)	34.9	15.4	4.2	135	61	5.2

Significance of the difference between the means (C.R.) of 20 normal controls, and 50 patients (35 E.S. and 15 anxiety states) on breath holding and leg raising tests.

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5. RESPONSE TO PERSISTENCE TESTS.

Two tests were adopted to test the subjects persistence in a setting of physical discomfort (a) breath holding and (b) leg raising.

For the breath holding test the patient was asked to stand, and at the top of a normal inspiration asked to hold his breath for as long as possible --- this was timed by stopwatch.

For the leg raising test, the patient lay on his back in bed and raised his left leg to half a right angle --- he was asked to maintain his leg in this position for as long as possible.

Material

20 normal controls including nine young doctors were used. Fifty patients were used, made up of 35 E.S. patients and 15 anxiety states.

Results.

Table 13 shows the results of the breath holding and leg raising tests. For the breath holding tests the mean of 20 controls was 57.0 sec. ± 21.2 S.D., and for the 50 patients 34.9 sec. ± 15.4 S.D. The difference between the two groups is significant c.r. 4.2; $P < .01$).

On the leg raising test 20 controls gave a mean of 312 sec. (5' 12") ± 147 S.D., and 50 patients a mean of 135 sec. (2' 15") ± 61 S.D. The difference between the two groups is significant c.r. 5.2; $P < .01$.

Discussion of Results of Persistance Tests.

The results of both tests indicate that the neurotic patients as a group lack persistence in the type of situation used for the test. The tests may well measure the same psychological factor as the maximal work, when the subject was asked to work on an ergometer to complete exhaustion. The tests here described are of course much simpler to carry out, and might prove to be a useful and rapidly carried out clinical test. Work still remains to be done however to determine what information the tests really provide.

6. OTHER FINDINGS

Previous work on the blood enzyme choline esterase which hydrolyses acetyl choline formed at the synapses of neurones (Tod & Jones (35)), suggested that a relatively high level of choline esterase was found in the blood of neurotic patients with autonomic overactivity. This work was later confirmed by Richter & Lee (39). We found that 112 E.S. patients gave a mean blood choline esterase of 98 units; this is significantly different to a group of 60 normal controls who showed a mean choline esterase of 79 units ($P < 0.01$).

Insulin tolerance tests (Fraser et al (36)) were done on 21 E.S. patients, 19 curves were essentially normal; in the remaining two cases the blood sugars were significantly below the fasting level after two hours; neither of these cases gave histories suggestive of spontaneous hypoglycaemic attacks, and there was no clinical evidence of pan-hypopituitarism. Facilities were not available for doing colorimitric assays of 17 - ketosteroids in the urine.

Fatigue is prominent among the symptoms of dictary deficiency particularly in relation to deficiencies of Vitamin B1, and C. Jolliffe et al (37) described a clinical picture indistinguishable from E.S. occuring in volunteers deprived of Vitamin B1. We studied (38) Vitamin B1 (excretion and saturation test), and Vitamin C (excretion and blood level) in 11 E.S. Group 2, and 10 E.S. Group 3. Vitamin C appeared to be low, but no lower than we found in normal subjects at that time of the year (winter). There was no evidence of Vitamin B1 deficiency in our patients.

APPLICATION OF OBJECTIVE FINDINGS TO THE TREATMENT OF EFFORT SYNDROME.

Treatment of most psychiatric conditions presents great difficulties because all too often the cause is not clear. At the beginning of the century the advent of the psycho-analytic method raised hopes that aetiological forms of treatment would be applicable to most psychiatric problems; these high hopes were not fulfilled, and there is no common agreement that psycho-analysis is the method of choice in more than a relatively small group of neurotic cases, and in few, if any, psychotic cases. Further the impracticability of a method which limits one therapist to treating 100 patients in a lifetime cannot be overlooked. More recently physical methods of treatment --- insulin-coma, E.C.T., and leucotomy in particular --- have given good therapeutic results in psychotic patients ~~in particular~~; here however, one is dealing with purely empirical procedures, and although much research has been stimulated, no important findings have yet resulted either as to the nature of the illnesses treated (mainly schizophrenia and depression), or the mode of action of the treatment. At present it is possible to hear one authority advocating psycho-analytic treatment(lasting 2 or 3 years) for a case of depression, and another authority advocating E.C.T. (lasting 2 to 3 weeks) for the same case. Obviously, the therapist is placed in a very difficult position when deciding on a course of treatment, but whatever his training and temperament may dictate, there can be no question that the more relevant facts collected about a case, the better balanced will be the course of treatment planned.

We started treating our E.S. patients and anxiety states at the beginning of the war with no fixed attitude towards proceedure. We were

a mixed group of physicians, psychiatrists, and research workers, and felt that many questions had to be studied, and if possible answered, before we were able to adopt any general orientation in treatment. Naturally we set about collecting clinical data from our psychiatric and physical examinations. The latter aspect of the problem has been very adequately covered by Paul Wood in his Goulstonian Lectures (1). The questions posed at the beginning of this thesis indicate the extent of our objective studies; the content of the thesis supplies the answers to these questions. How did all this help us in deciding on treatment proceedures? In severe cases of E.S. there was ample evidence from the symptoms and clinical signs that the subject was ill; milder cases however, were often difficult to distinguish from the hystero-malingerer; further we did not know if despite the symptoms we would be able to demonstrate by objective means a poor exercise response. Our studies showed us that these men as a group had a poor exercise response, but the complete understanding of the nature of this disability eluded us. Nevertheless, the nature of the symptoms and signs (palpitation, hyperpnoea, postural giddiness and fainting, left chest pain, tension headaches, cold blue hands, emotional sweating, etc.) all suggested that whatever the basic aetiological factor or factors in the condition were, vegetative imbalance was one accompaniment of the disturbance. Our studies of respiratory response to pain and cold, gave further objective evidence of this autonomic lability. Our enquiries had showed us that the E.S. patient <u>had</u> a disability - i.e.- a poor exercise response; further the response to maximal work showed that there was an effort phobia --- that the E.S. patient failed to drive himself to physiological end point, presumably for fear of the possible ill effects (to his heart) of excessively hard work. The patients themselves invariably attributed their condition to some physical disease --- almost always heart disease.

Repeated physical exams., X rays, and reassurance by cardiologists etc. had failed: they were told they had no heart disease, but how did that simple reassurance help them to deal with their palpitations, left chest pain, fainting etc., which after all were not imaginary? We soon realised that we had to educate these men so that they could come to realise the true meaning of their symptoms: only thus could they reasonably be expected to give up the idea of heart disease which the symptoms so strongly suggested. The lay public has a very limited catalogue of medical illnesses accumulated largely by hearsay and visiting relatives and friends in hospital: one of the few conditions which is commonly known and feared is 'heart disease', and it would be strange indeed if a layman assailed by palpitation and precordial pain failed to diagnose himself immediately --- in an age when most physicians are ignorant of psychosomatic medicine we cannot ask too much of the layman. But we soon found that to teach the physiological factors contributing to palpitation, breathlessness, left chest pain, tension headaches, postural giddiness and fainting, emotional fatigue etc., to individual patients made impossible demands on our time. So in 1941 we started taking the whole ward of up to 100 patients with E.S. as one group. Details of the method evolved would be too long to elaborate here (Jones (12) (43)). In brief, three hours of instruction were given each week --- a course covering twelve hours of instruction. In this way the course lasted one month, and as the average length of stay in hospital per patient was six to eight weeks, there were always some patients in the group who had had a complete 'course'. This was valuable, as our method was to let the patients themselves work out the mechanism of their symptoms -- e.g.-- the doctor would suggest that they should try to work out the mechanism of postural giddiness, and simply guide the ensuing discussion. We found this to be much the best educational proceedure for our particular needs, and it

was astonishing how articulate even a dull intellect could become. Most of the men had had mechanical training in the army, and enjoyed wrestling with the intricacies of human physiology. And the subject was interesting to practically everyone: our own studies of exercise physiology were referred to frequently and correlated with the exercise response of athletes as well as their own poor performances. Moreover most of the men had actually performed the tests and even helped in the laboratory in some capacity --- e.g. --- some excellant equipment was made for us by the patients. We drew freely from such fascinating studies as "Human Gastric Function" (Wolff and Wolff (40)), "The Wisdom of the Body" (W.B.Cannon (41)), and "Progressive Relaxation" (E. Jacobson (42)) as well as papers in the literature on fainting etc.

The subjects of the talks are the following:

1. The understanding of the voluntary nervous system, and it's functions in maintaining external harmony, e.g. you find a room too noisy, so you get out.
2. The understanding of the internal milieu, and the function of the involuntary nervous system in maintaining harmony.
3. The two parts of the involuntary nervous system, and possible combinations, i.e.- the sympathetic acting as a whole and the para- sympathetic acting in part.
4. Application of the previous two talks on external and internal harmony - e.g.- it is a hot day so what happens (a) in the thinking part of your brain? and (b) in the automatic part?
5. The understanding of fear (a) its physical and somatic aspects; (b) its teleological value; (c) its 'ordinariness'.
6. Nerves. Nervous tension. Muscle tension.
7. Relaxation. Anxious face. Awkward attitude. Restlessness in bed. Action potentials and thinking.
8. Left chest pain and breathlessness.

9. Circulation, cold blue hands, giddiness, fainting, blanching, blushing, etc. Homeostases and the efficient distribution of blood.

10. Nervous dyspepsia.

11. Fatigue, nervous and muscular; fatigue of activity and of inactivity.

12. Depression and insomnia.

The main advantages derived from these talks would appear to be:-

1. The patient is given an idea of anatomy and physiology, sufficient to allow him to objectify his symptoms.

2. The discussion of symptoms (which he may or may not have) in an impersonal manner also tends to produce an objective attitude towards his symptoms.

3. The conversation being on the patient's favourite topic ,i.e., Health, is of great interest to him.

4. The situation is an informal one, and the patients may be less tense than when being interviewed individually, and may therefore be presumed to be more receptive.

5. The group acceptance of a point has a strong suggestive value.

6. The patient's self - respect is considered; to give up his organ neurosis would entail a loss of prestige in his own eyes, and in those of the outside world. This is countered if he can give a reasonable explanation of the meaning of nervousness, and has a realisation of the enormous importance of this factor in medicine.

7. If he genuinely wants help he will be relieved to learn that no serious consequences need result from his symptoms.

8. The opportunity for raising health problems three times a week in open discussion leads to less health talk amongst the patients themselves, and, more important, leads to a more critical and informed attitude by his audience in the ward.

9. After a time the patients come to appreciate the 'ordinariness' of their

symptoms.

10. There is an enormous economy in doctors' time.

Our aim in these talks was not the elimination of symptoms, but a change of attitude towards the symptoms --- that they should no longer be attributed to heart disease etc., but understood as resulting from the autonomic accompaniments of emotional conflicts. Many of the patients (E.S. Group 2) had had a previous disability (poor exercise response) which they had simply accepted as a limitation, but under the stresses of the army in war time, this disability became an illness, the subject now showing a neurotic attitude towards his symptoms. Our aim was not to eliminate these symptoms, but to alter the mans attitude, and get him back to his previous rational acceptance of a slight disability. To achieve this it was usually necessary to either transfer him to lighter duties, not entailing violent physical exertion or discharge him from the army. The percentage of E.S. patients returned to the army was as follows:- 1941, 49%; 1942, 63%; 1943, 59%; 1944, 66%; Unfortunately no adequate follow up of this material is available, but the results must have been reasonably good, since a large percentage of failures would inevitably have been returned to Mill Hill as the main E.S. unit in the country.

In conclusion no attempt has been made to go into the treatment of E.S. in any detail. Our findings showed that E.S. is not a psychiatric diagnosis, and the usual psychiatric diagnosis should be used, with effort syndrome added in brackets. To discuss fully the treatment of E.S. would be to enter the troubled waters of psychiatric treatment in general. Our aim has been to collect objective information regarding a syndrome, the nature which was controversial, and apply this knowledge to the formulation of a treatment programme. It might be argued that a similar approach to the

selection of cases suitable for the various forms of physical treatment in psychiatry is desirable. By objective study of the vegetative and other physical characteristics of case material, certain significant factors might emerge which might correlate with some clinical finding -- e.g.-- the measurement of some attribute of 'tension' might aid the selection of suitable case for leucotomy; at present of two clinically similar depressions, one may respond favourably to the operation, and the other fail. Physical treatment methods certainly interfere with the body function, and they may well produce their effects by this change. We need such objective guides as our clinical sense is wrong all too often; further any such objective findings might throw some light on aetiology, and improve our treatment methods.

SUMMARY

1. EXERCISE RESPONSE to work done on a bicycle ergometer.

(a) Standard Work: (6,750 ft. lbs. of work per min. for 5 mins.)

A significant difference between a group of normal controls and groups of neurotic patients with various diagnoses was obtained by measuring the post exercise pulse response (pulse area), the post exercise oxygen uptake, and the blood lactate rise following exercise.

Post exercise ventilation showed no evidence of deficient ventilation, the volume per breath was approximately equal in controls, effort syndrome, (E.S.) ~~patients~~, and anxiety states, but in both groups of patients more ventilation was necessary for the assimilation of 100 cc of oxygen than in the controls.

(b) Maximal Work: (work to complete exhaustion)

Twenty normal controls showed a significantly greater blood lactate rise following maximal work than did a group of 20 E.S. patients. It appeared that the E.S. patients gave up before a 'physiological end point' had been reached or in other words that the E.S. patients had an effort phobia.

Arterial blood gas analysis gave no evidence of anoxaemia after maximal work; nor was there any evidence of respiratory alkalosis resulting from hyperventilation after maximal work, judged by the blood pH and pCO_2.

(c) Light Work: (4,500 ft. lbs. of work per min. for 1 min.)

A simple respiratory exercise tolerance test was devised using a closed circuit metabolism machine. Significantly greater ventilation post exercise was recorded in the group of E.S. patients compared with the controls.

(d) Minimal Work : (Pedaling against no resistance).

A work situation without any real work being done was created by asking

the subject to pedal the ergometer against no resistance. Respiratory tracings were obtained by using a closed circuit metabolism apparatus. The results showed a marked tendency in E.S. patients for irregular and/or excessive breathing to occur in a work situation.

The reason for the poor exercise response in neurotic patients was studied, but no definite conclusions were arrived at. An attempt to create experimentally a poor exercise response in a normal control showed that paralysing the vagus by intravenous atropine resulted in a greatly increased post exercise oxygen uptake; a much smaller rise resulted from voluntary hyperpnoea (simulating E.S. breathing) or the administration of adrenaline to the control before exercise. Neither muscle tension nor autonomic overactivity alone appeared to adequately explain the poor exercise response in neurotic patients.

2.&3. RESPONSE TO PAIN AND COLD

Blood pressure and respiratory responses to these two external stimuli were studied. Significant differences between certain groups of neurotics and normal controls were obtained when the increased ventilation resulting from the stimulus was measured. The B.P. response to the two stimuli showed no significant difference between controls and neurotic patients.

4. RESPONSE TO EXCITEMENT

The emotional excitement of the initial interview was used as a stimulus and pulse, respiratory, and B.P. readings taken at this time were contrasted with similar readings taken some weeks later under basal conditions. A possibly significant fall in pulse and B.P. readings occurred in certain groups of neurotic patients, but unfortunately no normal controls were available for comparison.

5. PERSISTANCE

Breathholding and leg raising tests were used and both tests showed

significant differences between groups of neurotic patients and normal controls.

6. OTHER FINDINGS

The enzyme choline esterase was found to be significantly higher in a group of E.S. patients when compared with a group of normal controls. It is suggested that blood choline esterase is higher in subjects with autonomic overactivity.

Insulin tolerance tests done on E.S.patients gave generally normal results.

We found no evidence of Vitamin B1 deficiency in E.S. patients on quantitative testing (excretion and saturation test). Vitamin C (excretion and blood level) appeared to be low, but no lower than we found in normal subjects at the same time of year (winter).

7. TREATMENT

The above objective findings were used to guide our formulation of a treatment programme designed to combat effort intolerance in E.S. patients. Education of the patient to an understanding of the meaning of his symptoms is considered to be the most important aim. Twelve hours of physiological and psychological talks were given each month to the whole group of E.S. patients. Cures were not expected, but rather a change of attitude by the patient towards his symptoms --- these whichpreviously had been regarded as an illness were now accepted without anxiety as an understandable physical disability. The wider question of the psychiatric treatment of the neurosis itself is not discussed as our concern is primarily with poor exercise response and the symptoms related to this.

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